REMARKS

As an initial matter, the Applicant notes that the election/restriction requirement mailed July 27, 2009 was made final. Applicant cancels claims withdrawn from examination without prejudice to Applicant's right to petition the restriction or to file a divisional application.

Regarding the Examiner's objection to claims 21 and 23 based on formalities, these claims are cancelled and the objection is now believed to be moot.

Regarding the Examiner's rejections of all claims (21 – 26 and 31) based on 35 USC §112, first and second paragraphs, all claims are cancelled. New claims are now submitted that distinctly (*i*) claim the process for protein production at a cultivation temperature below 25°C and (*ii*) claim the chaperonins as defined by their amino acid sequences. Applicant submits that all §112 based rejections are believed to now be moot because the application, inclusive of the new claims, fully satisfies the legal requirements of the written description as set forth in 35 USC §112, all paragraphs. The new claims are supported by the Applicant's original disclosure and no new matter is added. Therefore, Applicant requests that all §112 based rejections be withdrawn and the newly submitted claims are believed to be in condition for allowance.

New claim 32 is based on original claims 11 and 12, reciting the chaperonins of original claims 3, 6 and 7. Original claims 11 and 12 recite a process for heterologous protein expression in a host microorganism. The microorganism is cultivated at low temperatures (below 25°C) and broadly defined to include animal cells, plant cells, fungi, yeasts, and bacteria cells that can be characterized by the various DNA sequences for encoding different chaperonins. Newly submitted claim 32 focuses the scope of subject matter that patent protection is sought for. It distinctly claims (*i*) the process for protein production at a cultivation temperature below 25°C and (*ii*) the chaperonins as defined by their amino acid sequences. As explained below, claim 32 and the claims that depend from it are believed to be in condition for allowance.

The stabilized double ring mutant, recited in new claim 32, is defined by the amino acid sequence of Cpn60 with the mutation in positions 468 and 471. With respect to the chaperonins, claim 32 is now limited to Cpn60 and its specific mutants. In the

specification on page 10, 2nd complete paragraph, the Applicant states that Cpn60 and its variants are essential for producing protein in correct conformation at lower growth temperatures. Example 6 shows that native Cpn60 and the specific mutants of the present invention have a refolding activity at lower growth temperatures. The Applicant submits that Cpn60 is both essential and sufficient for heterologous protein expression at lower growth temperatures. Further, the host cells are limited to bacteria, namely to both Gram-positive or Gram-negative bacteria. For at least these reasons, Applicant believes new claim 32 is allowable. The co-chaperonin Cpn10 can bind to Cpn60 or its mutants, and is therefore recited in claim 33, which depends from claim 32. Claims 33 – 36 and 40 – 42 depend from claim 32 and are also believed to be allowable. Withdrawal of the rejections for indefiniteness and lack of enablement is requested.

New claim 37, based on original claims 14 – 18, is directed to the extracellular, or *in-vitro*, refolding process for changing the conformation of denatured proteins into their native conformation. Claim 37 recites a process that includes contacting the denatured protein with a functional chaperonin. Furthermore, the functional chaperonin is selected from the group already recited in new claim 32. Therefore, it is believed that these claims form one homogenous group that can be examined. Applicant believes the claimed subject matter satisfies the written description requirements of 35 USC §112 because there is a basis for claims 37 – 39 and 43 in the specification [pp. 2-3], in Example 6, and in original claims 14 – 18.

The Examiner contends that one skilled in the art would be required to undergo undue experimentation, in violation of 35 USC §112, first paragraph, to identify a nucleic acid encoding a variant of SEQ ID NO:1 or 2 that is capable of enhancing the growth of mesophilic host cells at low temperatures. The new claims are believed to sufficiently narrow the scope of patentable subject matter. The Examiner contends that the nature and breadth of the claimed invention encompasses a method of utilizing any nucleic acid encoding any functional variant Cpn60 and Cpn10 to express heterologous proteins in any host cell at a low temperature. New independent claims 32 and 37 are fully supported by the specification without addition of new matter, and Applicant believes these claims and the claims that depend from them are allowable. The

specification provides guidance and examples related to SEQ ID NO:1 and 2, expression of nucleic acid encoding SEQ ID NO: 1 and 2 in bacteria, such as *Oleispira antarctica* and *E. Coli,* the positive results when temperatures are low, as well as stabilized and unstabilized mutants of SEQ ID NO:6 and their expression.

The Examiner also contends that the claims recite subject matter of an undue breadth. The claims have already been restricted to Group III, relating to bacteria, in the election/restriction requirement referenced above. Addressing the issue of claiming host cells other than *E. Coli,* Applicant submits that the claims reciting the heterologous protein expression are now restricted to bacteria. Therefore, the Applicant believes the claims recite subject matter that is supported in the specification because the process as claimed and described is a predictable process when carried out in bacteria according to the claims as now submitted. For at least these reasons Applicant believes that all claims are now in condition for allowance.

Furthermore, as the present invention is based on the effect provided by chaperonins Cpn60 or its mutants, either during heterologous protein expression in a host cell, in which they are encoded, or in an in vitro refolding process of denatured protein, the invention is not dependent on the genus of the host cell. As the presence of Cpn60 or its mutants provides for the inventive effect of proper performance of proteins, e.g. also resulting in lower growth temperatures, the invention is not drawn to a genus of compounds which would include non-defined members. Therefore, Applicant submits that the host cell is only one vehicle for realizing or manifesting the invention. The experimental evidence provided for *E. Coli* is sufficient for showing that the invention is described in sufficient detail to be performed over the whole range of bacteria, as claimed.

Further, the skilled artisan will understand that the processes of the invention are enabled by the presence of Cpn60 or its variants as defined, which for the first time allow protein production by expression in a host cell at lower temperatures, or refolding of denatured protein in an in vitro process at lower temperatures, and therefore the processes do not depend on the specific selection of the host cell. In this respect it could further be emphasized that no state of the art document or evidence has been provided that would prove that the chaperonins could not be used in a specific bacterial

host cell.

To satisfy the enablement requirement, Applicant need not describe all actual embodiments. Proof of enablement would be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation. (MPEP §2164.02) Currently, no such reason is given by the Examiner. The Examiner has not shown that undue experimentation would be required. Applicant submits that there is no reason to believe that other bacteria would not work and would, therefore, not be within the scope of the present invention.

As an additional point, Applicant also addresses the statement on pages 6 and 7 of the July 27, 2009 restriction requirement for the sake of a complete record. The sequence discussed by the Examiner on pages 6 and 7 of the restriction requirement only contained the DNA and amino acid sequences of the natural chaperonins Cpn10 and Cpn60, and there is no suggestion of the biological activity of the chaperonins. The process of the new claims are distinguished based upon particularly claimed use of the biologically activity of Cpn60, and its ability to correctly fold protein at lower temperatures, both during cultivation at lower temperatures and in in vitro refolding processes of originally denatured protein. The biological activity was published by the inventors after the priority date of this application in Mol. Microbiol. 53(1) 167-182, published in 2004 after the 13 October 2003 priority date.

For the above reasons, withdrawal of the multiple rejections of all claims based on statutory requirements of 35 USC §112 is requested. New claims 32 – 43 are believed to be written so that they satisfy the statutory requirements of distinctly and clearly describing the claimed subject matter and providing enough support for a skilled artisan to be able to practice the present invention. Applicant respectfully requests consideration of the claims now submitted and believed to be in condition for allowance.

Respectfully submitted,

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